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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,297	01/04/2002	Hendrik Van Urk	P27,692 USA	9302

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EXAMINER

STRZELECKA, TERESA E

ART UNIT	PAPER NUMBER
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1637

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 09/890,297	Applicant(s) VAN URK ET AL.	
	Examiner Teresa E. Strzelecka	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 January 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 152-170 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 152-170 is/are rejected.
- 7) ☒ Claim(s) 163 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission filed on January 8, 2007 has been entered.

2. Claims 54-56, 59-92 and 95-151 were previously pending. Applicants cancelled claims 54-56, 59-92 and 95-151 and added new claims 152-170. Claims 152-170 will be examined.

3. Applicants' claim cancellation obviated the following rejections: rejection of claims 54-56, 59-67, 69-71, 74-81, 90-92, 95-102, 104-106, 109-115, 134-136, 141 and 142 under 35 U.S.C. 103(a) over Goodey et al. (WO 97/31947) and Matsuoka et al., as evidenced by Cohn et al., Shaklai et al. and Ohmura et al.; rejection of claims 68, 72, 73, 103, 107 and 108 under 35 U.S.C. 103(a) over Goodey et al. (WO 97/31947) and Matsuoka et al., as evidenced by Cohn et al., Shaklai et al. and Ohmura et al., and further in view of Ohmura et al. and Chang; rejection of claims 82, 84, 86, 88, 137 and 139 over Goodey et al. (WO 97/31947) and Matsuoka-1 et al., as evidenced by Cohn et al., Shaklai et al. and Ohmura et al., and Matsuoka-2 et al.; rejection of claims 83, 85, 87, 89, 138 and 140 over Goodey et al. (WO 97/31947) and Matsuoka-1 et al., as evidenced by Cohn et al., Shaklai et al. and Ohmura et al., Matsuoka-2 et al. and Chang; rejection of claims 116-121, 130-133, 143-145, 150 and 151 under 35 U.S.C. 103(a) over Goodey et al. (WO 97/31947) and Matsuoka et al., as evidenced by Cohn et al., Shaklai et al. and Ohmura et al.; rejection of claims 122, 123, 126, 127, 146 and 148 over Goodey et al. (WO 97/31947) and Matsuoka-1 et al., as evidenced by Cohn et al., Shaklai et al. and Ohmura et al., and Matsuoka-2 et al.; rejection of claims 124, 125, 128, 129, 147

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and 149 over Goodey et al. (WO 97/31947) and Matsuoka-1 et al., as evidenced by Cohn et al., Shaklai et al. and Ohmura et al., Matsuoka-2 et al. and Chang.

4. This office action presents new grounds for rejection.

Claim Objections

5. Claim 163 is objected to because of the following informalities: it is not clear from what claim this claim should depend, as currently it depends from itself. Appropriate correction is required.

Claim Interpretation

6. Before proceeding with art rejections meaning of some of the terms present in the claims, for which the definitions were not provided by Applicants, will be interpreted.

A) "Chromatography in the negative mode with respect to albumin" is interpreted to mean that albumin is not adsorbed onto the chromatographic matrix and is recovered in the flow-through, and "chromatography in the positive mode with respect to albumin" is interpreted to mean that albumin is adsorbed onto the chromatographic matrix.

B) The term "glycoconjugate" is interpreted as any glycosylated material, such as glycoproteins, glycopeptides, etc.

C) A note regarding rejection of the claims in which the order of steps was reversed: reversal of steps is considered to be prima facie obvious (see MPEP 2144.04 IV C).

MPEP 2144.04 IV

C. Changes in Sequence of Adding Ingredients

Ex parte Rubin , 128 USPQ 440 (Bd. App. 1959) (Prior art reference disclosing a process of making a laminated sheet wherein a base sheet is first coated with a metallic film and thereafter impregnated with a thermosetting material was held to render prima facie obvious claims directed to a process of making a laminated sheet by reversing the order of the prior art process steps.). See also In re Burhans, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing

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process steps is prima facie obvious in the absence of new or unexpected results); In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 152, 154-162 and 164-170 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goodey et al. (WO 97/31947; cited in the IDS and in the previous office action) and Johnson et al. (U.S. Patent No. 5,625,041 A).

A) Regarding claim 152, Goodey et al. teach a process for purifying an albumin solution, the process comprising:

(1) subjecting the albumin solution to cation exchange (CE) chromatography in the positive mode with respect to albumin in order to yield an albumin-containing CE product (Goodey et al. teach CE chromatography of an albumin solution on cation exchanger; see page 1, lines 26-31; page 2, lines 1-10);

(2) subjecting the albumin-containing CE product, with or without intervening purification step, to anion exchange (AE) chromatography to yield an albumin-containing AE product (Goodey et al. teach a process comprising CE and AE chromatography, with a possible steps of affinity chromatography (AC), ultrafiltration and gel permeation chromatography before AE chromatography; see page 2, lines 6-31; page 3, lines 1-16);

(3) placing the albumin-containing AE product, without further purification, into a final

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container for therapeutic use (Goodey et al. teach placing the purified albumin into a plurality of vials (page 6, lines 28-30) and placing the albumin solution into a bulk product formulation vessel, followed by completing formulation by addition of pharmaceutically acceptable excipients (page 27, lines 20-22).); and

wherein the albumin solution subjected to the cation exchange chromatography step that is run in the negative mode with respect to albumin has an albumin concentration of $10\text{-}250\text{g.L}^{-1}$ (Goodey et al. teach adjusting the concentration of albumin between different purification steps to within the specified range (page 21, line 8; page 23, line 25; page 24, line 23; page 32, lines 10 and 25; page 33, line 21; page 37, line 10; page 39, line 9).

Regarding claims 154 and 155, Goodey et al. teach adjusting albumin concentration between different purification steps to within the specified range (page 21, line 8; page 23, line 25; page 24, line 23; page 32, lines 10 and 25; page 33, line 21; page 37, line 10; page 39, line 9).

Regarding claims 156, 158, and 159, Goodey et al. teach adjusting the pH of albumin solution and conditioning of albumin solution by addition of octanoate salt prior to cation exchange step (page 3, lines 20-22; page 16, lines 9-11).

Regarding claim 157, Goodey et al. teach a process comprising CE and AE chromatography, with a possible steps of affinity chromatography (AC), ultrafiltration and gel permeation chromatography before AE chromatography (page 2, lines 6-31; page 3, lines 1-16).

Regarding claims 160 and 161, Goodey et al. teach initial albumin solution with octanoate concentration of 1-10 mM (page 3, lines 20-22; page 16, lines 9-11).

Regarding claims 164 and 168, Goodey et al. teach AE step run in a positive mode with respect to albumin (page 25, lines 9-29).

Regarding claim 165, Goodey et al. teach the pH of albumin solution applied to anion

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exchange column of 4.5-6.0 (page 25, line 18).

Regarding claim 166, Goodey et al. teach fermentation before albumin purification (page 10, lines 12-31; page 11-15).

Regarding claim 167, Goodey et al. teaches a process for purifying an albumin solution, the process comprising the steps of:

(i) subjecting an albumin solution to a CE chromatography step run in positive mode with respect to albumin (Goodey et al. teach CE chromatography of an albumin solution on cation exchanger; see page 1, lines 26-31; page 2, lines 1-10; page 21, lines 1-26);

(ii) collecting an albumin-containing CE eluate (Goodey et al. teach collecting 6.5 volumes of eluate; page 21, lines 26-28);

(iii) subjecting the CE eluate to an AE chromatography step run in a positive mode with respect to the albumin (Goodey et al. teach AE chromatography run in a positive mode with respect to albumin; page 25, lines 9-26);

(iv) collecting an albumin-containing AE eluate (Goodey et al. teach collecting albumin-containing eluate; page 3, lines 4-16; page 25, lines 27-29);

(v) subjecting the AE eluate to an affinity chromatography (AC) step run in positive mode with respect to the albumin (Goodey et al. teach AC chromatography of albumin on a column containing a matrix which specifically binds albumin, such as DBA (Delta Blue Agarose) matrix; page 22; page 23, lines 1-20);

(vi) collecting the albumin-containing AC eluate (Goodey et al. teach collecting the AC eluate; page 3, lines 4-16; page 23, lines 16-20);

(vii) subjecting the affinity chromatography eluate to an affinity chromatography step run in negative mode with respect to albumin and in positive mode with respect to glycoconjugates

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(Goodey et al. teach PBA column chromatography for binding glycoconjugates (page 36, lines 11-30; page 27, lines 1-18);

(viii) collecting the albumin-containing affinity chromatography flow-through (page 37, lines 8-21).

Regarding claim 170, Goodey et al. teach adjusting the pH of albumin solution and conditioning of albumin solution by addition of octanoate salt prior to cation exchange step (page 3, lines 20-22; page 16, lines 9-11).

B) Goodey et al. do not teach albumin purification using CE or AE chromatography run in a negative mode with respect to albumin.

C) Johnson et al. teach albumin purification using CE and AE chromatography in a negative mode with respect to albumin to remove albumin-binding compounds from the protein solution (Abstract; col. 2, lines 1-67).

It would have been *prima facie* obvious to one of ordinary skill in the art to add the CE and AE chromatography steps run in a negative mode with respect to albumin of Johnson et al. to the albumin purification method of Goodey et al. The motivation to do so, provided by Johnson et al., would have been that using ion exchange in negative mode with respect to albumin removed dyes which are used in the process of protein purification (col. 2, lines 17-67), and Goodey et al. teaching using such dyes in albumin purification (page 4, lines 10-19), and, as stated by Johnson et al. (col. 4, lines 33-42):

“It is to be noted that, although the process of the invention is particularly well suited to separating a protein-binding compound from a protein when the protein-binding compound has been used to purify the protein from, for example, a fermentation medium or a product thereof, the process can generally be used to separate any suitable protein-binding contaminant from a protein.

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An advantage of the process is that it does not require binding on the protein to the resin and hence relatively large volumes of protein can be purified for a given volume of resin.”

Therefore, the teaching of Johnson et al. regarding the ion exchange purification enhances the ability of Goodey et al. to obtain highly purified albumin therapeutic treatments (Goodey et al., page 1, lines 1-25).

9. Claims 153 and 163 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goodey et al. (WO 97/31947; cited in the IDS and in the previous office action) and Johnson et al. (U.S. Patent No. 5,625,041 A), as applied to claim 152 above, and further in view of Fisher et al. (U.S. Patent No. 4,228,154; cited in the IDS and in a previous office action).

A) Neither Goodey et al. nor Johnson et al. teach albumin solution subjected to cation exchange mode with respect to albumin to have a pH of 4.5-6.0 or albumin solution which undergoes anion exchange chromatography to have pH of 4.0-5.2.

B) Regarding claims 153 and 163, Fisher et al. teach purification of albumin using cation and anion exchange chromatography run in the negative mode with respect to albumin (col. 2, lines 19-50).

Regarding claim 153, Fisher et al. teach adjusting the pH before loading onto cation exchange column to between 4.5-4.9 (col. 2, lines 24-28).

Regarding claim 163, Fisher et al. teach adjusting the pH before loading onto anion exchange column to between 5.1 and 5.5 (col. 2, lines 29-33).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the pH values of Fisher et al. in the method of Goodey et al. and Johnson et al. The motivation to do so, provided by Fisher et al., would have been that at these pH values albumin did not bind to either the cation or the anion exchanger, respectively (col. 2, lines 36-38).

10. No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E. Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Teresa E Strzelecka
Primary Examiner
Art Unit 1637

Teresa Strzelecka
3/19/07